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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,109	03/30/2004	Michael W. Salter	2560.004	5534

21917 7590 09/11/2006

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,109	SALTER ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-5,11,13-15,19-25,30,36-39 and 44-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10,12,16-18,26-29,31-35,40-43 and 47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/04&9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II (claims 6-10, 12, 16-18, 26-29, 31-35, 40-43, and 47-49) in the reply filed on 6/30/06 is acknowledged. The examiner further acknowledges, as noted by Applicant, that claims 16-18 belong in group II as well.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Priority is to the instant application, which was filed 3/30/04.

Information Disclosure Statement

3. Ingman et al (page 2, of ids filed 9/05) has been considered. However, in the absence of an alignment with a sequence of the instant application, the examiner cannot assess the relevance of the reference.

Claim objections

4. Claims 9-10, 17-18, 29, and 33-35 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the

above claims, Applicant recites an intended use (i.e., for cells of a CNS..) which does not further structurally limit the ***composition*** claimed.

5. Claim 6 is objected to because of the following informalities: It contains reference to 'SUDAPI,' without first disclosing the meaning of the acronym. In order to make the description of the invention more clear, the first claim that mentions these acronyms should fully express the phrase, and be followed by parentheses, which identify the acronym to be used in the following claim(s). Amendment of claim 6 to include 'SUDAPI' in parentheses right after the term 'Src unique domain anchoring protein inhibitor,' would overcome the rejection. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 6-10, 12, 16-18, 26-29, 31-35, 40-43, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition of polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for a for '***modifiying***' NMDA receptor interaction with Src comprising at least one '***SUDAPI.***', or for a pharmaceutical composition of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

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The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a generic 'sudapi' inhibitor that works by *modifying* an *intracellular* interaction between Src and NMDA in neurons of the brain or peripheral nervous system. The generic inhibitor must be capable of transport across the blood brain barrier and further transport across the plasma membrane of the target neuron. The invention is complex because the specification provides *one* sequence coupled to HIV-TAT that *inhibits* Src-NMDa interaction, but the invention claimed is to *any (structurally undefined)* compound that *modifies* Src-NMDA interaction, and is capable of delivery into the intracellular environment of neurons in the brain and peripheral nervous system (PNS).

The prior art does not recognize a 'sudapi,' and does not recognize compounds that enhance Src-NMDA interaction (which is reasonably encompassed by 'modifying'). The prior art recognizes coupling of HIV-TAT to polypeptides (but not generic sudapi compounds) for brain/neuron delivery (see Schwarze et al, 1999). However, the prior art does not recognize that polypeptides such as SEQ ID NO: 1 can be delivered

effectively to the brain and intracellular environment of a neuron without HIV-TAT or another known protein transport domain. Therefore a "pharmaceutical composition' comprising SEQ ID NO: 1 is not supported.

The working examples show that the composition comprising SEQ ID NO: 2 is useful for *inhibiting* interaction between Src and NMDA, and for treating pain in an animal model of pain. The working examples do not support any other molecule, or generic 'sudapi' for modifying or inhibiting the interaction between Src and NMDA.

The breadth of the claims are such that they include unknown and undisclosed 'sudapis' that 'modify' Src-NMDA receptor interaction. Further, there is no guidance as to how to make a sudapi, let alone make a sudapi that 'modifies' Src-NMDA receptor interaction.

Therefore, given the complex nature of the invention, the lack of support in the prior art, and the lack of examples or guidance, one skilled in the art would not be able to make or use the invention as currently claimed.

5. Claims 6-10, 26-29, and 32-35 are rejected under 35 U.S.C. 112; first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to unknown and undisclosed molecules called 'sudapis.' The claims do not require that the compounds possess any particular biological activity

except modifiying the interaction between Src and NMDA, nor do generic 'sudapis' have any particular conserved structure, or other disclosed distinguishing feature. Therefore, there are no clear structural limitations on the complex of molecules claimed. Thus, the claims are drawn to a broad functionally-defined genus that lacks any structural definition.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. In the instant application, no such distinctions have been made. One polypeptide has been disclosed, SEQ ID NO: 2, which is not sufficient to characterize the broad class of compounds claimed. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Applicant has described one polypeptide.

.Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed

above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of compounds and therefore conception is not achieved until reduction to practice has occurred.. Adequate written description requires more than a mere statement that it is part of the invention. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polypeptides described in the specification have sufficient written description, and not generic 'sudapis.' Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6-10, 12, 16-18, 33-35, and 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 16 describe a pharmaceutical composition for 'modifying' Src-NMDA receptor interaction comprising a 'sudapi.' 'Modifying' reasonably includes inhibiting and activating or facilitating. Thus the claims encompass any manner of

altering said interaction. However, Applicant defines 'sudapi' as 'Src unique domain anchoring protein ***inhibitor***,' which reasonably does not activate or facilitate the interaction it simultaneously inhibits. Claims 7-10, 17-18, 33-35, and 40-43 are rejected because they depend from the indefinite claims 6 and 16.

Claim Rejections - 35 USC § 102/103

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 6, 9-10, 26 and 29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gingrich et al., 2001, Society for Neuroscience abstract, entitled "ND2, A Mitochondrially encoded protein, interacts with SRC Kinase at the NMDA receptor complex."

Gingrich et al teach Src peptide 40-58 corresponding to the instant peptide of SEQ ID NO: 1, which is Src peptide aa 39-47. Gingrich et al al report that Src40-58 disrupts Src tyrosine kinase modulation of NMDA receptor activity and indicate that it does so by inhibiting Src-NMDA interaction (see abstract). Therefore Gingrich is a SUDAPI. The Src peptide is disclosed as used in an epitope-tagged binding assay. This assay (and others) was undoubtedly performed in an aqueous solution, which meets the limitation of "pharmaceutically acceptable solution" in the rejection under

102(b). Alternatively, it would be obvious to solvate the peptide in an aqueous solution because that is how nearly all peptides are stored in solution.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-10, 26-27, 28-29, and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gingrich et al as applied to claims above, and further in view of Schwarze et al (1999).

Gingrich discloses a 'SUDAPI' polypeptide that blocks the interaction between Src and NMDA as described above under 35 USC § 102(b).

Gingrich et al does not disclose coupling the peptide to HIV-TAT protein so that the polypeptide can be carried across the blood brain barrier or into the intracellular space of neurons,

Schwarze et al. teach delivery of a protein, beta-galactosidase, into brain cells of a mouse by conjugation with the HIV TAT protein (-YGRKKKRRQRRR-' see page 1572, bibliography, #7). See figure 4, wherein Scharze et al show that TAT collects in the cell bodies of CA-3 pyramidal neurons (page 1572).

One of ordinary skill in the art would be motivated to combine the method of Ginigrich et al with the HIV TAT sequence of Schwarze et al because it would allow delivery of the competitive peptide Src unique binding domain sequence (SEQ ID NO: 1) to neurons in the brain and CNS to block the interaction between Src and NMDA.

The motivational statement is further given by Schwarze et al. stating "These results open new possibilities for direct delivery of proteins into patients in the context of protein therapy...[abstract]"

One of ordinary skill would have a reasonable expectation of success in delivery of the peptide to the intracellular environment of CNS/PNS neurons because Schwarze et al suggest HIV TAT would be useful for treatment for *any* therapeutic protein, including those that must be targeted to the brain (abstract).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
8/30/05

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER